## REMARKS/ARGUMENTS

The specification has been amended to correct the typographical error, as pointed out by the examiner at paragraph No. 4 of Paper No. 5, and to assign the SEQ ID NOS: to the amino acid sequences that have not previously been assigned with a sequence identifier, as required by the Sequence Rules. A new Sequence Listing that was amended with the addition of the newly created SEQ ID NOS: is also submitted. No new matter is believed to be introduced as these sequences have been disclosed in the original specification of the present application.

**Claims 59 and 60 have been objected to by the examiner because they depend from the non-elected claims 58 and 54, respectively.**

Claim 60 has been amended to include the limitations of claim 54. Claim 59 has been canceled. This objection therefore should be obviated by these amendments.

**Claims 59-63 have been rejected by the examiner under 35 U.S.C. § 101.**

The examiner asserts that a credible utility for the claimed invention can not be assessed. Reconsideration under 37 CFR 1.111 is requested.

The applicants respectfully submit that the claimed invention, a sGNK polypeptide, has a well established utility, i.e., for use in the regulation or treatment of angiogenesis or vascularization. According to the USPTO's Revised Interim Utility Guidelines Training Materials, (http://www.uspto.gov/web/menu/utility.pdf), issued in 1999, a well established utility is "a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art." (Page 7) (Emphasis added). The applicants submit that the asserted utility for sGNK is specific, substantial, and credible. It is "specific" because sGNK has been discovered by the applicants as a physiological substrate of GNK, a kinase which plays a critical role in angiogenesis and vascularization. Moreover, this utility is specific because it is not a utility that can be applied generically to any proteins, such as a protein supplement for animal food, as illustrated in the Utility guideline. The applicants further submit that this utility is "credible" because, according to the Utility guideline, "[a]n assertion is credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon

which the assertion is based are inconsistent with the logic underlying the assertion." (Page 5) (Emphasis added) The specification discloses the role of GNK in vascularization, in particular the data shown in Figure 11, which clearly show that vascularization is greatly reduced in the yolk sacs from mice that are deficient of GNK compared to those from mice that are GNK positive. In view of this disclosure, Applicants thus submit that the logic underlying the utility assertion is neither seriously flawed nor inconsistent with the facts. The applicants further submit that the asserted utility is also "substantial" because it defines a "real world use." Since the utility is connected to angiogenesis and vascularization regulation – a real world use – it is not a "throw away" utility that would apply to virtually every protein.

In view of the preceding discussion, the applicants respectfully submit that the examiner has applied an improper standard for her conclusion that the claimed invention does not have a well established utility. To support her conclusion the examiner asserts that (1) further experimentation is needed (to show a similar observation in human of the data shown in Figure 10, i.e., animal data), and (2) that the asserted utility is not supported by or inconsistent with the degree of sequence homology between human sGNK and the *Drosophila* bicaudal-D protein and human c-Nap1. This is not proper because these two reasons are <u>not</u> evidence that would doubt the asserted utility (discussed below); they are merely allegations that the examiner made based on her knowledge of science and patent law given the applicants' disclosure. First, the examiner required human data that would show a similar if not the same observation obtained with animal experimentation that is shown in Figure 11. This requirement is not proper as the examiner appears to raise the utility standard to the drug approval standard required by the U.S. Food and Drug Administration. As reiterated in *In re Brana*, 51 F.3d 1560, 34 USPQ2d at 1437 (Fed. Cir. 1995), using experimentation animals is sufficient to establish utility. Regarding the degree of homology to the bicaudal-D protein of *Drosophila*, the applicants respectfully submit that the examiner is erred in making the conclusion that, "[s]ince the specification repeatedly states that sGNK is associated somehow with vascularization and angiogenesis, it would not be expected that the homology to the Bicaudal-D gene of Drosophila could be extrapolated to the function of that [sic] sGNK because the functions of the claimed protein and bicaudal-D are <u>clearly different</u>." (Emphasis added) (Paper No. 5, page 6). The examiner appears to take a position that

since sGNK is associated with vascularization and angiogenesis and that the Drosophila bicaudal-D protein is described as to be associated with cytoskeleton, mRNA sorting and polarity of developing embryo, their functions are different; thus establishing the role of sGNK in vascularization is inconsistent. The applicants respectfully submit that the observations made and disclosed by the applicants on sGNK and the bicaudal-D protein are not inconsistent; they suggest that GNK, and by implication, sGNK, may function to regulate cytoskeletal dynamics that affect endothelial cell growth, migration or adhesion, processes that are known to be involved with vascularization. Not only has the examiner failed to demonstrate that the logic underlying the asserted utility is seriously flawed, or that the facts are inconsistent with the logic; the examiner has also failed to provide evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility. *In re Brana*, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995).

Even assuming *arguendo* that the reasons provided by the examiner may be considered as such evidence, the applicants respectfully submit that the examiner can not make this type of rejection unless it has reason to doubt the objective truth of the applicants' statement in the specification. *In re Cortright*, 165 F.3d 1353, 49 USPQ2d 1464 (Fed. Cir. 1999). Thus the only reasonable conclusion that could be reached based on the applicants' disclosure is that the asserted utility is well established. The withdrawal of this rejection is therefore respectfully requested.

**Claims 59-63 have been rejected by the examiner under 35 U.S.C. § 112, first paragraph.**

The examiner asserts that since the claimed invention is not supported by a well established utility, as set forth in the preceding rejection, one skilled in the art would not know how to use the invention. The examiner also further asserts that even if these rejections (utility and enablement) are to be overcome, the claims would still be rejected because of the scope non-enablement under 112/1, first paragraph. Reconsideration under 37 CFR 1.111 is requested.

The applicants reiterate the arguments made in response to the rejection under 35 U.S.C. § 101, as set forth in the preceding discussion and respectfully request that the rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

Regarding what appears to be the examiner's additional rejection made under 35 U.S.C. § 112, first paragraph, i.e., an enablement scope rejection, reconsideration under 37 CFR 1.111 is requested. The examiner asserts that the specification, while being enabling for an isolated polypeptide comprising SEQ ID NO:2, does not reasonably provide enablement for (1) an isolated polypeptide with at least 80% identity to SEQ ID NO:2 which is capable of binding to and/or being phosphorylated by GNK, (2) a polypeptide produced from a nucleic acid capable of hybridizing to SEQ ID NO:4 (GNK) under conditions of moderate stringency, or (3) polypeptides comprising fragments of SEQ ID NO:2.

The examiner asserts that even if sGNK activity is as same as that of Bicaudal or c-Nap1, "it is well known in the art that protein chemistry is probably one of the most unpredictable areas of biotechnology." Page 9 of Office action. The examiner further asserts that the differences in amino acid sequence between the broadly claimed polypeptides and SEQ ID NO:2 can not be predicted, citing five references to support for this unpredictability assertion.

Before providing a response to this rejection, the applicants respectfully submit that the examiner has mischaracterized the claims in making this rejection. Specifically, while the examiner recites the polypeptides of (1) above are capable of binding to and/or being phosphorylated by GNK, she does not recite the same functional limitation to the polypeptides of (2) and (3) above. Since all the polypeptides are recited with the same functional limitation, the applicants will respond to the examiner's rejection in view of these limitations.

The applicants respectfully submit that the claims are enabled because they can be practiced without "undue experimentation." *In re Wands*, USPQ2d 1400 (Fed. Cir. 1988). The key word here is "undue," not experimentation," as stated in *In re Angstadt* (190 USPQ 214 (C.C.P.A. 1976)) and reiterated in *Wands*. According to *Wands,* "whether undue experimentation is needed is not a single, simple factual determination, bur rather is a conclusion reached by weighing many factual considerations." *Wands* went on to reiterate the factors that must be considered in determining undue experimentation, which was summarized in *Ex parte Forman* (230 USPQ 547). These factors include: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the

state of the prior art, (6) the relative skill of those in the art, (7) the predictability of the art, and (8) the breadth of the claims. Based on this guidance, the applicants respectfully submit that the examiner has not provided an adequate basis in accordance to these factors when making this rejection. This deficiency notwithstanding, the applicants submit the reasons why the applicants clearly satisfy the standard for enablement as articulated in *Wands*, which are as follows.

With respect to the amino acid identity limitation (i.e., at least 80% identical to SEQ ID NO:2), the applicants teach a wide variety of variants that include the polypeptides that are at least 80% identical to SEQ ID NO:2, and how to make them. For example, see pages 14-17 of the specification.

With respect to the other limitation of the claims, that these polypeptides are capable of binding to and/or being phosphorylated by a GNK polypeptide having SEQ ID NO:4, the applicants also teach how to determine such limitation. See pages 45, Example 3 "Kinase assay demonstrating autophosphorylation of GNK and phosphorylation of sGNK by GNK."

With respect to the examiner's cited publications in support for the non-enablement position, the applicants submit that the teachings of these publications are not applicable in the context of the instantly claimed invention. While the instant claims recite a polypeptide variants of sGNK, which have the limitations that are specific to sGNK that can be determined by the teaching of the specification, these cited references, on the other hand, individually discuss either an unknown protein or a protein which is not related to sGNK.

Thus one skilled in the art, guided by the applicants' disclosure, can make the polypeptides as claimed. Consequently, the applicants respectfully submit that the claims satisfy the Federal Circuit's standard for enablement and request that the scope rejection be withdrawn.

**Claims 61 and 63 have been rejected by the examiner under 35 U.S.C. § 112, first paragraph, as the specification allegedly does not contain a written description of the claimed invention.**

Reconsideration under 37 CFR 1.111 is requested. The examiner asserts that the polypeptides recited in paragraph (c) of claim 61, are not supported by the specification

as originally filed, specifying that the fragments of the claimed polypeptides only have support for having at least 20 or at least 30 amino acids in length, not for as broad as instantly claimed. The applicants respectfully submit that the fragments that are cited by the examiner should be considered to be additional to the fragments that are disclosed at the outset of the section titled, "Polypeptides and Fragment Thereof." Page 13, line 12. This is supported by the expression in the paragraph where the fragments of at least 20 or 30 amino acid long are discussed, which is started with the language, "Also provided herein are polypeptide fragments comprising at least 20, or about at least 30, contiguous amino acids of the sequence of SEQ ID NO:2 or SEQ ID NO:4." Page 14, line 10. (Emphasis added)

Based on the reasons as stated by the examiner to support this rejection, the applicants respectfully submit that the rejection appears to be more of a new matter rejection, not the written description-type rejection that is discussed in the USPTO's Synopsis of Application of Written Description Guidelines, (http://www.uspto.gov/web/menu/written.pdf). Even if the examiner intended to make the rejection as discussed in the Guidelines, the applicants respectfully submit that the examiner has not made a *prima facie* case of lack of written description by presenting evidence or reasons why one skilled in the art would not recognize in the disclosure a description of the invention defined by the claims. *In re Alton*, 37 USPQ2d 1578 (Fed. Cir. 1996). Accordingly, the applicants respectfully request the rejection be withdrawn.

**Claims 59-61 have been rejected under 35 U.S.C. § 102(a) as being allegedly anticipated by Ishikawa et al.**

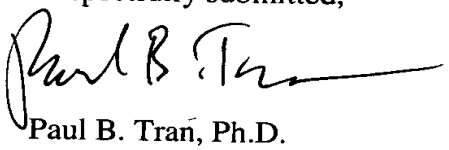
Reconsideration under 37 CFR 1.111 is requested. In response to this rejection, the applicants submit herewith a Rule 131 Declaration signed by all the inventors. The declarants describe the nucleic acid and amino acid sequences of human sGNK prior to 1998, the publication year of cited reference. Accordingly, the applicants submit that they have broadly established a completion of an embodiment of the invention prior to the date of the cited reference. In view of the 131 Declaration, the applicants respectfully request the examiner to withdraw this rejection.

**Claim 63 has been rejected under 35 U.S.C. § 103 as being allegedly unpatentable over Ishikawa et al. in view of US Patent No. 5,968,781 (Yoon et al.).**

Reconsideration under 37 CFR 1.111 is requested. The applicants respectfully request the examiner to withdraw this rejection because the primary reference, Ishikawa et al., is not a proper reference under 35 USC § 102 or § 103. As presented in the response to the § 102(a) rejection, Ishikawa et al. has been antedated by the applicants' 131 Declaration. The only reference remained in this rejection is Yoon et al. Although Yoon et al. may teach a histidine-tagged polypeptide and the purification thereof, it does not teach or suggest sGNK, or any amino acid sequence variants thereof.

Applicants respectfully request that a timely Notice of Allowance be issued for this case.

Respectfully submitted,



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